until a short tubular tract lined with mucosa is formed. Why this fixation of the deepest portions should occur, permitting, the normal depth of the lower lip to develop, is of course conjectural."

The treatment of the fistulæ, when treatment is indicated, is by excision.

A CONTRIBUTION TO THE ETIOLOGY OF PERNICIOUS ANEMIA.[1]

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In 1860 Flint published his inferences regarding the atrophy of the stomach mucosa in cases of pernicious anemia. Ten years later Fenwick actually demonstrated the gastric lesion and worked out its pathology. Quinke, in 1876, was, however, the first, I believe, to consider the gastric changes as the causative factor of the anemia, while Martius, Lubarsch, and Koch considered the pathological findings in the stomach and intestines as secondary factors.

We appreciate now, however, that some hemolytic agent is present in the blood, and various theories have been advanced as to its origin. Hunter, in 1890, seems to have been the first to recognize this, and believed that some toxin was produced in the stomach in certain cases which was responsible for the hemolysis. Much pathological research was done to isolate this ptomain, and in 1898 Schauman, Faust, and Tallquist recovered a lipoid substance from the segments of the bothriocephalus, which when administered to animals reproduced a blood picture resembling closely that of pernicious anemia. This they considered either a sodium or cholesterin combination with oleic acid.

Ten years later, in 1909, Berger and Tsuchyia extracted a lipoid substance from the gastric and intestinal mucosa of patients who had died from pericious anemia, which showed hemolytic properties ten times stronger than extracts obtained in other conditions. They further reproduced, by animal injection of this extract, an anemia of the pernicious type.

Faber, who has probably made the most searching studies of the gastro-intestinal pathology in this disease, states that the changes noted in most intestines are postmortem, and will not be found present if the part is preserved immediately after death, but that the atrophy in the stomach is constant, and that in the stomach the etiologic factor must be sought for.

Herzberg, in a careful pathological study of 9 cases, concurs with Faber and believes that the gastric and blood phenomena in pernicious anemia arise from the same cause.

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It is with the hope that some light may be thrown on this etiologic factor that the following observations are presented.

In the analysis of 433 cases of abdominal complaint presenting the symptoms of achlorhydria hæmorrhagica gastrica, most of which were observed at the Mayo clinic, there occurred during 1909, 1910, 1911, 34 cases of pernicioûs anemia. All cases of pernicious anemia presented the findings of an achlorhydria hæmorrhagica gastrica. Two cases of pericious anemia examined one year before the blood dyscrasia evidenced itself showed lack of free hydrochloric acid and the presence of occult blood in the stomach extract. Many of them gave long histories of chronic digestive disturbances before there was any blood change, but no stomach analysis is recorded. Several developed marked paresthesia of the extremities when their blood showed as yet only a slight secondary anemia, with no evidence of a pernicious character.

Of the 433 cases of achlorhydria examined, 149 were operated on as they presented definite intra-abdominal disease. Gross pathological findings in these showed involvement of the appendix in 52 cases; the gall-bladder in 57 cases; the gall-bladder and pancreas in 21 cases, and the stomach in 19 cases. There were 19 cases in which the gall-bladder was diseased concomitantly with the appendix.

The anamnesis in 156 of the remaining cases developed the fact that the onset of gastric symptoms seemed to bear an immediate and direct relation to various diseases and conditions, among which the incidence of infectious diseases in 38 cases, circulatory disturbances in 12, postoperative development in 14, and derangement of the ductless glands in 20 instances, deserve mention.

Appreciating generally the extraordinary degree of gastric disturbance which irritation in distant organs can produce, it may be considered even more than a presumptive conclusion that reflex nervous phenomena are responsible primarily for the inhibition of the production of hydrochloric acid in these cases.

The bacterial flora present in cases of achlorhydria hæmorrhagica, achylia gastrica, and pernicious anemia are identical. Streptococci, colon, diplococci, lactic acid, staphylococci, proteus, and leptothrix are present in great numbers. Frequently all varieties may be seen in the same field so great is their profusion. In several instances the cells of the mucosa itself had taken on phagocytic properties. A chemical analysis can be foretold almost without exception from this picture of the bacterial flora under the microscope, and ample control of these observations by repeated examination of the flora existing in cases of hyperacidity, normal and hypoacidity, and in malignant and non-malignant stenoses seem to justify the following conclusions:

That in the stomachs of patients presenting the symptoms of lack of free hydrochloric acid there is present a very large number of bacteria. Varieties ordinarily pathogenic are almost universally found either alone or in combination; that their presence is dependent upon the lowered acidity of the gastric juice, that they are actively growing bacteria, evidenced by their profusion, morphological characteristics, and staining properties; that the streptococci are probably the most important factors, since they are found in large numbers in those cases where pus was noted.

My interest in this question of the bacterial content in the stomach in cases of achlorhydria and pernicious anemia was lately stimulated by an article by McCaskey, who was able to obtain from the blood cultures, streptococci in each of the cases of pernicious anemia examined by him, in two of which administration of an autogenous vaccine appeared to be instrumental in overcoming streptococcemia, and further remarks that all the cases in which fever was present in whom blood cultures were made, showed the presence of streptococci. This was significant when one appreciates that fever occurs in approximately 80 per cent. of cases of pericious anemia. In further analyzing this phenomenon we find it continuing at times for weeks, or recurring periodically, but absent during the remissions which so frequently occur, and when, as Moffitt has noted, in certain cases of high temperature, profound exhaustion, nervous phenomena, and an enlarged spleen are noted they speak strongly in favor of an infective agency.

Fejes has demonstrated that anemia may be produced experimentally by bacterial hemolysins. Toxins produced by certain strains of streptococci have been shown to be distinctly hemolytic.

When one reflects upon the various means employed to treat pernicious anemia, the fact must seem apparent that possibly unconsciously they have all been working empirically to effect the same result, namely, the cleansing of the gastro-intestinal tract by the administration of medicines which we have lately learned to be germicidal in their action. Thus intestinal lavage, appendicostomy with colonic irrigation, administration by mouth of intestinal antiseptics, lavage of the stomach, thorough evacuation of the bowels, arsenic in its various forms, as Fowler's solution, and intravenous injections of salvarsan, autogenous vaccines, and finally hydrochloric acid.

I wish then to present for consideration these facts, namely:

1. Achlorhydria is merely a symptom denoting a marked degree of chronic gastritis.
2. It is usually evoked through extragastric irritative factors which are in many instances capable of correction.
3. There are, without exception, present in such stomachs great numbers of bacteria ordinarily considered pathogenic, among which streptococci are especially to be noted.

4. Practically all recorded cases of authenticated pernicious anemia present the symptom of achlorhydria, and in my own series of thirty-four cases the presence of occult blood in the stomach extract.

5. Thirty-four instances of pernicious anemia were noted in patients presenting the symptom of achlorhydria hæmorrhagica gastrica.

6. In a few of these cases the lack of hydrochloric acid and the presence of occult blood were known to be present at least one year before any blood changes were to be noted. In others the phenomena of paresthesia were evidenced some time previous to blood impairment, and many had suffered for years from chronic gastro-intestinal complaints.

7. Eighty per cent. of cases of pernicious anemia have increased temperature some time during the course of the disease.

8. Pure cultures of streptococci have been found by competent observers in the blood of patients with pernicious anemia who were running a fever.

9. Bacterial hemolysins are known to produce anemia resembling the pernicious type, as are other toxic substances, among which may be classed the lipoid group.

10. Efforts directed to the control of bacterial growth in the body and particularly in the gastro-intestinal tract have caused complete remissions in this disease in some instances.

11. The phenomena of occurrence, remission, and re-occurrence of the blood picture characteristic of pernicious anemia may be explained by our present knowledge of the action of toxins from whatever source, impairing the formation of antibodies until a bacteremia is produced which may be clinically recognized.

12. The toxins we have present being eliminated by the profuse flora in the gastro-intestinal tract, the impairment of bodily resistance is accomplished through their absorption and the disturbance of digestion in cases of achlorhydria.

13. Finally, reactive and combative ability of patients suffering with achlorhydria varies in different patients, and on this ground alone might be explained the relatively rare occurrence of pernicious anemia, although the occurrence of achlorhydria is fairly common.

Thus the development of pericious anemia would seem to be dependent upon a personal idiosyncrasy of certain individuals, in fact we must revert for the real etiologic factor of its inception to an embryonic tendency, the presence of which we are not as yet able to determine until it has been stimulated into an active destructive agent of the blood by the toxins absorbed from the profuse bacterial flora present in the stomach.